FORM PTO-1390 (REV 5-93) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 410.016

U.S. APPLICATION NO (If known, see 37 CFR 1.5): 09/308195

INTERNATIONAL APPLICATION NO	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/FR97/02336	December 17, 1997	December 23, 1996

TITLE OF INVENTION: METHOD AND SYSTEM FOR QUALITY MANAGEMENT IN THERAPEUTIC PROCESSES

APPLICANT(S) FOR DO/EO/US: THIBAULT et al

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
3. [ ] This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. [ ] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [X] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] has been transmitted by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US)
6. [X] A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. [ ] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [ ] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. [XX] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [XX] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [XX] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.
14. [ ] A substitute specification.
15. [ ] A change of power of attorney and/or address letter.
16. [XX] Other items or information: Verified Statement Claiming Small Entity Status-Small Business Concern; PCT/IPEA/416; PCT/IPEA/409; PCT/IPEA/408; Annexe; PCT/IPEA/429; PCT/IPEA/428WP; Reponse; Replacement Claims (3 pages); Drawings (7 sheets)

U.S. APPLICATION NO (If known, see 37 C.F.R. 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
	PCT/FR97/02336	410.016

17. [X] The following fees are submitted:

	CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5)): Search Report has been prepared by the EPO or JPO ..... $830.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) ..... $640.00 No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) ..... $710.00 Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37CFR 1.445(a)(2)) paid to USPTO..... $950.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4)..... $90.00	$ 970.00	
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 970.00	
Surcharge of $130.00 for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

Claims	Number Filed	Number Extra	Rate		
Total Claims	-20 =		X $22.00	$	
Independent Claims	-3 =		X $74.00	$	
Multiple dependent claims(s) (if applicable)			+ $230.00	$	
TOTAL OF ABOVE CALCULATIONS =				$ 970.00	
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$ 485.00	
SUBTOTAL =				$ 485.00	
Processing fee of $130.00 for furnishing the English translation later the [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +				$	
TOTAL NATIONAL FEE =				$ 485.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property +				$ 40.00	
TOTAL FEES ENCLOSED =				$ 525.00	
				Amount to be: refunded	$
				charged	$

a. [X] A check in the amount of $525.00 to cover the above fees is enclosed.

b. [ ] Please charge my Deposit Account No. _____ in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 02-2275. A duplicate copy of this sheet is enclosed

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:
Bierman, Muserlian and Lucas
600 Third Avenue
New York, NY 10016

SIGNATURE

Charles A. Muserlian
NAME

19,683
REGISTRATION NUMBER

Form PTO-1390 (REV 5-93)

VERIFIED STATEMENT CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) & 1.27(c))--SMALL BUSINESS CONCERN

Docket Number (Optional): 410.016

Applicant or Patentee: Eric THIBAULT and Jean-Loup ROMET-LEMONNE
Serial or Patent No.: PCT/FR97/02336
Filed or Issued: December 17, 1997
Title: METHOD AND SYSTEM FOR QUALITY MANAGEMENT IN THERAPEUTIC PROCESSES

I hereby declare that I am

- [ ] the owner of the small business concern identified below:
- [X] an official of the small business concern empowered to act on behalf of the concern identified below:

NAME OF SMALL BUSINESS CONCERN I.D.M. IMMUNO-DESIGNED MOLECULES
ADDRESS OF SMALL BUSINESS CONCERN 172, rue de Charonne
F-75011 Paris, FRANCE

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 13 CFR 121.12, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees to the United States Patent and Trademark Office, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention described in:

- [ ] the specification filed herewith with title as listed above.
- [X] the application identified above.
- [ ] the patent identified above.

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights in the invention must file separate verified statements averring to their status as small entities, and no rights to the invention are held by any person, other than the inventor, who would not qualify as an independent inventor under 37 CFR 1.9(c) if that person made the invention, or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d), or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern or organization having any rights in the invention is listed below:

- [ ] no such person, concern, or organization exists.
- [X] each such person, concern or organization is listed below.

Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING Jean-Loup ROMET-LEMONNE
TITLE OF PERSON IF OTHER THAN OWNER Executive Vice-President
ADDRESS OF PERSON SIGNING 172, rue de Charonne, F-75011 Paris, France
SIGNATURE [signature] DATE April 14, 1999

Our Ref.: 410.016

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	:	
THIBAULT et al	:	
PCT/FR97/02336	:	
Serial No.:	:	PCT Date: December 17, 1997
Filed: Concurrently Herewith	:	
For: METHOD AND SYSTEM FOR QUALITY MANAGEMENT IN THERAPEUTIC PROCESSES	:	
	:	
	600 Third Avenue New York, NY 10016	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Please amend this application as follows:

IN THE CLAIMS:

Claim 3, line 1, cancel "one claims 1 or 2" and insert --claim 1--.

Claims 5 to 8, line 1 of each, claims 12 and 13, line 3 of each, and claim 14, line 2, cancel "any one of the previous claims" and insert --claim 1--.

REMARKS

The amendment is presented to conform the claim dependency to the American practice. The Examiner should examine claims 1 to 14

on the replacement pages and not original claims 1 to 15.

Respectfully submitted,
BIERMAN, MUSERLIAN AND LUCAS

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CAM:sd
Enclosure: Return Receipt Postcard

"Method and system for quality management in therapeutic processes"

DESCRIPTION

The present invention relates to a process for quality management in therapeutic processes. It also relates to a system for its implementation.

The new therapeutic protocols involved at the level of cells and genes require a high level of reliability and security owing to the complexity of the operations carried out, the number of stages and personnel involved in the protocol. The quality requirement is even more crucial as these new therapies relate to the elementary blocks of human beings and are moreover the subject of justified vigilicance on the part of health authorities. It is moreover essential to guarantee total tracability of samples.

Cell therapy kits, for example the MAK™ kit produced by the company IDM, are currently finalized for supply to the laboratories in charge of treating cell samples taken from patients for whom clinicians have prescribed this therapeutic protocol. The cells treated in this way are reinjected into these patients.

In these therapeutic processes, both biological elements and physical objects are treated: the sample bags each associated with a patient and information: data associated with these bags and which indicate, in particular, the operators and the process state of progress.

The stages of treatment of the bags of cells are subjected to Standard Operating Procedures (SOPs) which are fully codified. Observance of these procedures ensures the quality of treatment required in order to be approved. However, the complexity of these procedures, the participation of several entities which are partners in the treatment processes, the need to rationalize the management of the increasingly automated therapeutic processes and the wish for vigilance expressed by the health authorities have led to the observation that it is not possible to segment responsibility for the management of therapeutic process

quality while counting only on each individual participant in the therapeutic process.

The document US 5 307 262 describes a process and system for quality management of clinical data related to patients. The process is implemented in the form of a computer program controlled by menus and in particular envisages data input concerning a patient, the entry of a command launching the quality control of this data, the displaying on screen of possible messages resulting from these controls, and if the operator judges this to be necessary, the provision and printing of one or more worksheets including messages that the operator chose from a menu, intended to facilitate the correction of data by the person or persons concerned (for example a specialist).

The document WO 94 27238 describes a testing system for microbiological specimens, including at least one workstation linked/connected to a database containing information relating to patients and a microbiological database. In particular, this system envisages the attribution of an identification number allowing access to the database and to link each tested specimen with the information relating to the patient concerned, the input of data relative to the test performed on the specimen using screen pages and the provision of a report.

The document US 5 072 303 describes a processing system for instructions and prescriptions within a hospital environment, including in particular the automatic updating of a task list in response to instructions or orders issued by the hospital doctors or nurses.

The purpose of the invention is to propose a quality management process which guarantees total consistency in the search for security and tracability throughout the different stages of the therapeutic process.

This objective is achieved with a process for the management of quality in a therapeutic process, this therapeutic process comprising the stages of taking cells from a patient, a specific treatment of these cells using a

specific treatment protocol, and reinjection into the patient of said cells treated in this way.

According to the invention, the process comprises:

- stages of identification of the entities involved in the therapeutic process,

- stages of sequential and conditional validation of the stages of the therapeutic process, and

- stages of quality control in which data acquired during said validation stages are processed in order to supply information on the quality of the realization of said therapeutic process, said stages of identification, validation and control being carried out for each batch of samples taken from a given patient.

In this way, with the process according to the invention, it becomes possible to provide checking and follow-up of complex therapeutic processes involving several entities and requiring total tracability.

A major advantage of the quality management process according to the invention in fact resides in the fact that it is based on the idea that a batch is associated with each patient, and that this batch and its associated data must be followed throughout the process. In particular, the standard operating procedures (SOP) can be followed and validated, ensuring a high level of tracability, reliability, and security.

When the quality management process according to the invention is implemented in a therapeutic process involving

several entities, optionally remote, and is associated with a standard operating procedure for preparation comprising a series of functional stages, this process then preferably comprises:

- stages of validation respectively associated with each of the functional stages, the passing from one validation stage to the following validation stage being conditional on the results of the processing of data collected during this validation stage, and

- a stage of processing of the information and data collected in the different validation stages, in order to issue final certification of a preparation carried out according to the standard operating procedure and/or a list of the anomalies detected during the preparation.

In a preferred implementation of the invention, validation of the final certification is conditional on the input of a validation password.

The quality management process according to the invention is advantageously implemented in the form of software installed on a data processing system. With each validation stage is associated at least one screen page which can be accessed on the display means of at least one workstation connected to the data processing system.

Each screen page comprises a coded identification field for a patient which matches the batch of samples subjected to the standard operating procedure.

It can advantageously be envisaged for the exit from certain stages of the process to be conditional on printing the screen pages corresponding to these stages.

In the case of a quality management process implemented in a preparation laboratory receiving therapeutic kits from at least one operational entity, this process then further comprises stages for monitoring the transfer of these kits.

When the preparation laboratory deals with a cytapheresis service, the quality management process further comprises stages for monitoring the receipt of cytapheresis pouches.

According to another aspect of the invention, a quality management system is proposed for the implementation of the process according to the invention. The functions of this quality management system can further be extended to include the management of other sectors of the preparation laboratory involved in the therapeutic process. Moreover, this system is preferably connected to a communications network, open or closed, for exchanging data with other entities involved in a therapeutic process.

The invention relates to a quality management system allowing the setup of other similar therapeutic protocol preparation processes and then their control and management within the same system.

Further features and advantages of the invention will appear in the description below. In the attached drawings, given as non-limitative examples:

- Figure 1 shows a quality management system according to the invention organized around one operator;

- Figure 2 shows a quality management organization involving several therapeutic processes;

- Figure 3 shows the different stages of a therapeutic process with which a quality management process according to the invention is associated;

- Figure 4 shows the essential stages of the software implementing the quality management process according to the invention;

- Figure 5 is a schematic representation of a screen page providing access to all the quality management stages;

- Figure 6 is a schematic representation of a screen page corresponding to a stage of preparation of an autologous serum;

- Figure 7 is a schematic representation of a screen page corresponding to a stage of bacteriological control;

- Figure 8 is a schematic representation of a screen page corresponding to a stage of quality control test result input;

- Figure 9 is a schematic representation of a screen

page corresponding to a stage of retrospective analysis;

- Figure 10 is a schematic representation of a screen page corresponding to a stage of final certification;

- Figure 11 is a schematic representation of a screen page corresponding to a stage of listing anomalies; and

- Figure 12 is a schematic representation of a screen page corresponding to a stage of transfer from the preparation laboratory to the treatment centre.

There follows a description of an example of implementation of the process according to the invention, in the area of cell therapy.

The parties involved in the operation of the process according to the invention are, with reference to Figure 1:

- an entity EX controlling operation of the process according to the invention and distributing the therapeutic kits KT,

- treatment centres CT, CTi, CTn run by clinicians CL, CLi, CLn who, for their patients PA, PAi, PAn, take the initiative of starting therapeutic protocols,

- preparation laboratories L1, Li, Ln which prepare, analyze and pack the products used in these therapeutic protocols,

- cytapheresis services CY, CYi, CYn which take samples from patients and make reinjections into them,

- bacteriological testing laboratories CB, CBi, CBn, and optionally collection centres CR separate from the operational entity EX.

The main stages of the therapeutic process controlled by the quality management process according to the invention are specified in several examples schematically illustrated in Figure 1.

In a first configuration encountered in the operation of the process according to the invention and described sequentially in Figure 3,

- 1/ a clinician CL in charge (0) of a patient PA within a treatment centre CT, issues a diagnosis DI and decides to contact a preparation laboratory L1 in order to start one or

more protocols intended for his patient,

- 2/ this laboratory L1 then contacts the operational entity EX for the therapeutic protocol process for it to supply it with the therapeutic kits corresponding to this protocol,

- 3/ the laboratory L1 also contacts a cytapheresis service CY with a view to organizing taking a plasma sample from the patient; a sample PR is taken from the patient;

- 4/ the laboratory L1 receives the therapeutic kit KT and an associated cytapheresis sheet from the operational entity EX or from a collection centre; the standard operating procedure(s) (SOP's) is/are then initiated,

- 5/ the laboratory L1 receives sample pouches from the cytapheresis service CY;

- 6/ the contents of these pouches are treated (TR) by the laboratory according to a standard operating procedure SOP and under the control of the quality management process according to the invention,

- 7/ then, when a final certification F is granted, the treated pouches accompanied by the necessary documents are sent to the clinician who arranges reinjection RI into the patient,

- 8/ post-reinjection follow-up information is input (7') and forwarded to the operational entity EX.

The operational entity is at the heart of the therapeutic process and manages the quality control and guarantees the tracability which is essential for this type of operation. The quality management process is intimately linked to the operating procedure SOP1 implemented in the laboratory L1, but it can also be involved in the management G of this laboratory.

In another possible operating configuration of the quality management process according to the invention, part of the entities involved in the therapeutic process are integrated on a single site. In this way, the laboratory Li in charge of the preparation can for exemple include the treatment centre CTi and its clinicians CLi in charge of

patients PAi and of the cytapheresis services CYi, the bacteriological control being carried out by an external laboratory CBi. The quality management process according to the invention can then be implemented both to follow up the operating procedure SOPi and to provide quality management Gi within the other entities CYi, CTi.

It can also be envisaged for the distribution of the therapeutic kits not to be directly carried out by the operational entity Ex but assigned to a collection centre CR with which a preparation laboratory Ln is in contact for the supply of the kits. The quality management process according to the invention then handles the follow-up of the procedure SOPn and the management Gn of this preparation laboratory which is also in contact with a bacteriological control laboratory CBn, a cytapheresis laboratory and one or more treatment centres CTn to which the clinicians CLn and their patients PAn are attached. The operational entity Ex receives from each preparation laboratory the information relating to the quality management of the operating procedures and post-reinjection monitoring. This data is processed, analyzed and optionally forwarded to a supervising authority AT.

The process according to the invention can be implemented for the quality management of several therapeutic protocols, as illustrated in Figure 2.

Several therapeutic protocols can be operated by an equivalent number of operational entities EXa, EXb each controlling a network Ra, Rb of preparation laboratories $L_{a,1}$, $L_{a,2}$, $L_{a,3}$, $L_{a,i}$, $L_{a,i+1}$, $L_{a,N}$; $L_{b,1}$, $L_{b,2}$, $L_{b,3}$, $L_{b,i}$, $L_{b,i+1}$, $L_{b,i+2}$, $L_{b,M}$. These laboratories carry out preparations for the treatment centres CT of patients PA and are all equipped with software implementing the quality management process according to the invention. The operational entities EXa, EXb supply the laboratories with therapeutic kits, provide supervision of the preparation operations carried out by the laboratories, collect quality management data and report for exemple to a supervising authority AT.

The data processing tools implemented with the quality management process can furthermore provide other control and processing functions, as illustrated in the diagram in Figure 4. In this way, the quality management process according to the invention offers the operator a command bar BC which provides access in particular to the following features:

- a Guide feature, which comprises a set of information on the techniques implemented in the therapeutic process, in particular in the form of animated sequences SA, SA1, SA2,.., SAm or of video sequences;

- a full sequential follow-up of the standard operating procedures (SOPs) which constitute the heart of the software embodying the process according to the invention; this software element EL comprises in particular a set of screen pages PO, PE1,.., PEn which are consulted sequentially and filled in by the operator;

- management and archiving DB of the data collected during the operation of the quality management process;

- management LM of the preparation laboratory which can include stock management SM, personnel management PM including in particular training requirements and ongoing appraisal of this personnel,
input/output management OM, and automated management GM of the standard operating procedures;

- a network feature NM for managing communications between the laboratory L1 and the other entities involved in the therapeutic protocols, in particular with bacteriological control laboratories CB, with treatment centres CT, with cytapheresis services CY, an operational entity EX, a collection centre CR and a connection XT to other networks.

There follows a description of the main stages of the quality management process according to the invention, with reference to the corresponding screen pages encountered by operators. It is here considered that the quality management process according to the invention is implemented in the form of software installed on an I.T. workstation in a preparation laboratory.

When the process according to the invention is launched, access is controlled using known techniques in this field, for exemple a request for a password and a check on this; the password or code can be regularly validated by self-assessment tests on the user's knowledge using an interactive program.

The operator is then prompted, on a home page, to supply identification data for the different parties involved in the therapeutic process with which the control process according to the invention is associated.

As a non-limitative example, in the case of the MAK™ cell therapy protocol, the operator is asked for information on the following entities:

- the clinician,
- the laboratory in charge of the preparation of the MAK™ protocol,
- the laboratory in charge of the bacteriological control,
- the laboratory in charge of the apheresis,
- the treatment centre.

With each request for information on an entity participating in the protocol is associated a screen page the critical points of which must be completed in full by the operator before being allowed to pass to the following screen page, for security and tracability reasons. It is to be noted that each screen page contains a coded identification of a patient.

There follows a description of several exemples of screen pages designed for each of the stages of the SOP module of the quality management process according to the invention, with reference to Figures 5 to 12. Only a limited number of screen pages which are characteristic of the process are shown below.

A screen page PO (Fig. 5) provides the process operator with a table of contents E and the details RM of the laboratory in charge of the preparation, in particular the name LA of this laboratory, its postal address AD, its

telephone number TL, fax number FA and E-mail address EM as well as the name CL of the person in charge of preparations. The screen page PO also contains the preparations' start date DD and end date DF, and identification fields which are essential for the quality management process according to the invention;

- the study title ST,
- a batch number LN,
- an apheresis barcode number BC,
- a "patient" code CP.

This screen page PO, in fact like all the screen pages developed for the process according to the invention, uses a graphic interface and the different parts E1, E2, ..., Ei, ...En of the software can be selected using a mouse. The screen page can be closed using a cancellation command CA. The information can be entered using the keyboard, the mouse, vocally or by any other input means allowing the operator to work in appropriate operating conditions, in particular aseptic conditions.

After a screen page (not illustrated) corresponding to the parameters for the collection stage of a treatment kit, the quality management process operator must complete a screen page PEi corresponding to the preparation of an autologous serum. This screen page comprises, as a non-limitative example, a title EP, a reminder of the patient code CP and of the date D, and a series of operational instructions S1, S2, ..., Sj, ...Sn which must be carried out in sequence. Data entered by the operator can be associated with each of these instructions. When all of these operations have been carried out, selection of a validation key VA orders the page to be closed, which is only confirmed if all the instructions have been carried out.

Bacteriological control stages are envisaged throughout the preparation process. The screen page EB (Fig. 7) corresponds to one of these bacteriological control stages. It generally comprises a header containing a title EC, a reminder of the study ST, of the patient code CP and of the

date D, a module RM indicating the details of the laboratory responsible for the preparation and the batch number LN, and a module BS containing the data relating to the bacteriological control, in particular the address AB of the laboratory in charge of the bacteriological control, an indication OB of the control operator, the results TB of a set of bacteriological control tests and the date DB of these tests. This screen page EB further comprises an indication AL that printing of this screen page is mandatory. A print command icon PR is provided for this purpose.

When all the stages of the standard operating procedure SOP have been executed, a screen page ER lists all the results of the quality tests which must be entered by the operator. This screen page ER comprises a similar header containing a title PR, a reminder of the patient code CP and the operation date D, and a table listing a series of quantitative tests CT with each of which is associated a "result" field RE which must be completed by the operator, and a "standards" field containing the maximum and minimum values constituting the standards. An icon BA allows the operator to return to the previous screen pages.

A retrospective analysis screen page EA (Fig. 9) must be completed by the operator once the treated cells have been reinjected. This screen page EA contains a header including a stage title RA, the patient code CP and the date D, and a table listing, for a set EXA of tests PH, CX, CS, BS carried out after reinjection, the results RE which must be entered by the operator and, opposite each result, the corresponding standard NO.

Final certification of a preparation is obtained from a specific screen page EC (Fig. 10) which, in addition to the identification header containing a title FC, the patient code CP and the date D, comprises a declaration CF of final certification providing significant quantitative and qualitative results RF specific sizes and physiological characteristics CF: number of cells, viability, percentage, sterility. There follows a declaration of final

certification DC in which there is an indication Yes (Y) or No (N) of whether final certification has in fact been granted to this preparation. An alarm icon AI prompts the operator to consult a screen page EI (Fig. 11) listing the anomalies detected during the process. On the final certification screen page EC, a specific icon PC allows the operator to pass to the screen page ET (Fig.12) for the transfer of the preparation to the treatment centre. Moreover, a print command PR, a validation command VA and a cancellation command CA are normally provided. It is to be noted that this certification screen page EC can only be validated after a password has been entered and checked, for reasons of certification security.

The anomalies screen page EI comprises a header including a title LI, a reminder of the patient code CP, of the date D, of the study ST and of the batch number LN. There follows a list I1-I4 of anomalies detected during the process with an indication of the remedies which have been applied. This screen page EI further comprises an indication NI of the number of anomalies checked and an indication TI of the total number of anomalies. A message IN prompts the operator to consult the screen page corresponding to a given anomaly by double clicking on the required anomaly using the mouse. After optional consultation of this anomalies screen page, the operator can then consulter and process the screen page ET for transfer to the treatment centre. In addition to a header including a title, this screen page comprises a reminder of the patient code CP, of the study ST and of the date D, on the one hand a set of data LAB characteristic of the laboratory responsible for the preparation, and on the other hand the details TC of the treatment centre to which the preparation is destined.

The characteristics LAB include, for the laboratory, the name LA, the postal address AD, the telephone and fax numbers TL, FA, and the name CL of the person in charge of the preparation. The information TC relating to the treatment centre includes its title TR, its address AD, its telephone

and fax numbers TL, FA and the name PI of the person in charge of this treatment.

A message MA warns the operator that this screen page must be printed, further comprising, for example at the bottom of the page, information relating to transmission and reception operations. In this way, the transmission EN and reception ER lines must be completed by the operator for the following fields: dates DS, DR; times TS, TR and persons in charge PS, PT.

Of course, the invention is not limited to the examples which have just been described and numerous developments can be added to these exemples without exceeding the scope of the invention. In this way, this process can be applied to the control and follow-up of quality in many fields other than that of cell therapy. It can moreover be integrated into laboratory automation processes. The process according to the invention also takes account of current concerns relating to biological vigilance and pharmacological vigilance.

CLAIMS

1. Process for the processing of information used for the management of quality in a therapeutic process, this therapeutic process comprising the operations of taking cells (PR) from a patient (PA), specific treatment operations on these cells using a specific treatment protocol, and a reinjection operation into the patient of said cells treated in this way, these operations of taking cells, treatment and reinjection being subjected to a standard operating procedure for preparation (SOP) comprising a series of functional stages,

characterized in that it comprises, for each batch of samples taken from a given patient:

- for each functional stage, a stage of sequential and conditional validation (VA) of said stage, the passing from one validation stage to the following validation stage being conditional on the results of the processing of data collected during this validation stage, and
- a stage of processing of the information and data collected in the different validation stages, in order to issue final certification (CF) of a preparation carried out according to the standard operating procedure and/or a list of the anomalies detected during this preparation.

2. Process according to claim 1, characterized in that validation of the final certification is conditional on the input of a validation password.

3. Process according to one claims 1 or 2, implemented in a data processing system, characterized in that with each validation stage is associated at least one screen page (PO, Pei, EP, EA, EC, EI) which can be accessed on the display means of at least one workstation connected to said data processing system.

4. Process according to claim 3, characterized in that each

screen page comprises a coded identification field for a patient which matches the batch of samples subjected to the standard operating procedure.

5. Process according to any one of the previous claims, characterized in that the exit from certain stages (RA) of said process is conditional on printing the screen pages (EA) corresponding to these stages.

6. Process according to any one of the previous claims, implemented in a preparation laboratory receiving therapeutic kits from at least one operational entity (EX), characterized in that it further comprises stages for monitoring the transfer of these kits.

7. Process according to any one of the previous claims, implemented in a preparation laboratory which deals with a cytapheresis service, characterized in that it further comprises stages for monitoring the receipt of cytapheresis pouches.

8. Process according to any one of the previous claims, implemented in a preparation laboratory which deals with a control laboratory, in particular a bacteriological control laboratory, characterized in that it further comprises stages for processing the results of control tests carried out on each batch of samples.

9. System for the processing of information used for the management of quality in a therapeutic process, this therapeutic process comprising the operations of taking cells (PR) from a patient (PA), specific treatment operations on these cells using a specific treatment protocol (SOP), and a reinjection operation (RI) into the patient of said cells treated in this way, these operations of taking cells, treatment and reinjection being subjected to a standard operating procedure for preparation comprising a series of

functional stages (TR),
characterized in that it comprises, for each batch of samples taken from a given patient:
- for each functional stage, a means of sequential and conditional validation (VA) of said stage, the passing from one validation stage to the following validation stage being conditional on the results of the processing of data collected during this validation stage, and
- a means of processing of the information and data collected in the different validation stages, in order to issue final certification (CF) of a preparation carried out according to the standard operating procedure and/or a list of the anomalies detected during the preparation.

10. System according to claim 9, implemented in a preparation laboratory, characterized in that it is further designed to execute management tasks (GN) within this laboratory.

11. System according to claim 9, characterized in that it is connected to a communications network in order to exchange data with other entities (CTn, Ln, Cyn, CRn, CB) involved in a therapeutic process.

12. Application of the process and of the information processing system used for quality management according to any one of the previous claims to cell therapy protocols.

13. Application of the process and of the information processing system used for quality management according to any one of the previous claims to gene therapy protocols.

14. Application of the process and of the quality management system according to any one of the previous claims, allowing ongoing training of the operator and/or the monitoring of his or her level of knowledge.

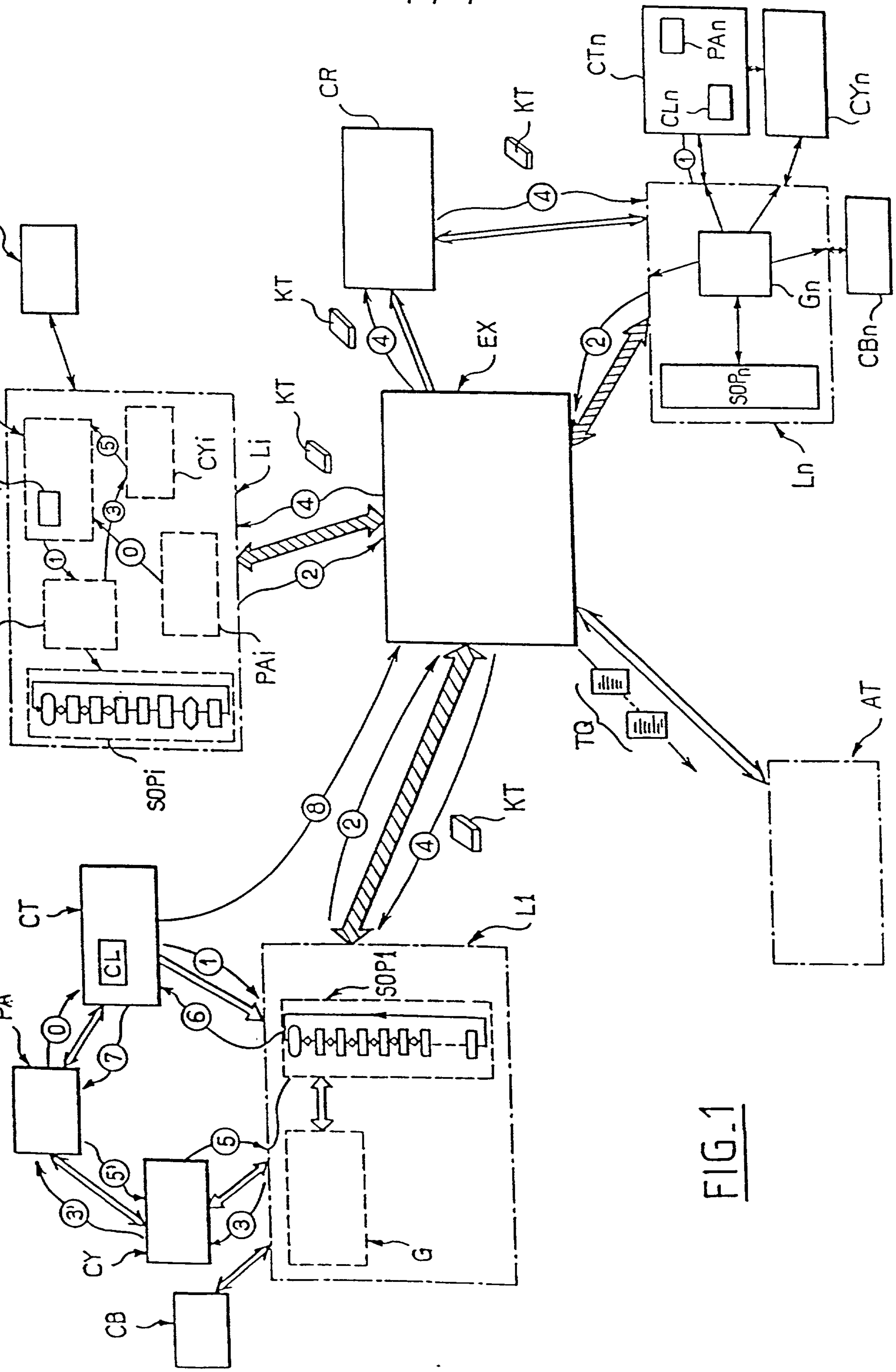
CT
CL
PA
CY
CB
G
L1
SOP1
EX
CR
KT
CTi
CLi
CYi
Li
Gi
PAi
SOPi
CBi
CTn
CLn
PAn
CYn
Gn
CBn
Ln
SOPn
AT
TQ

FIG.1

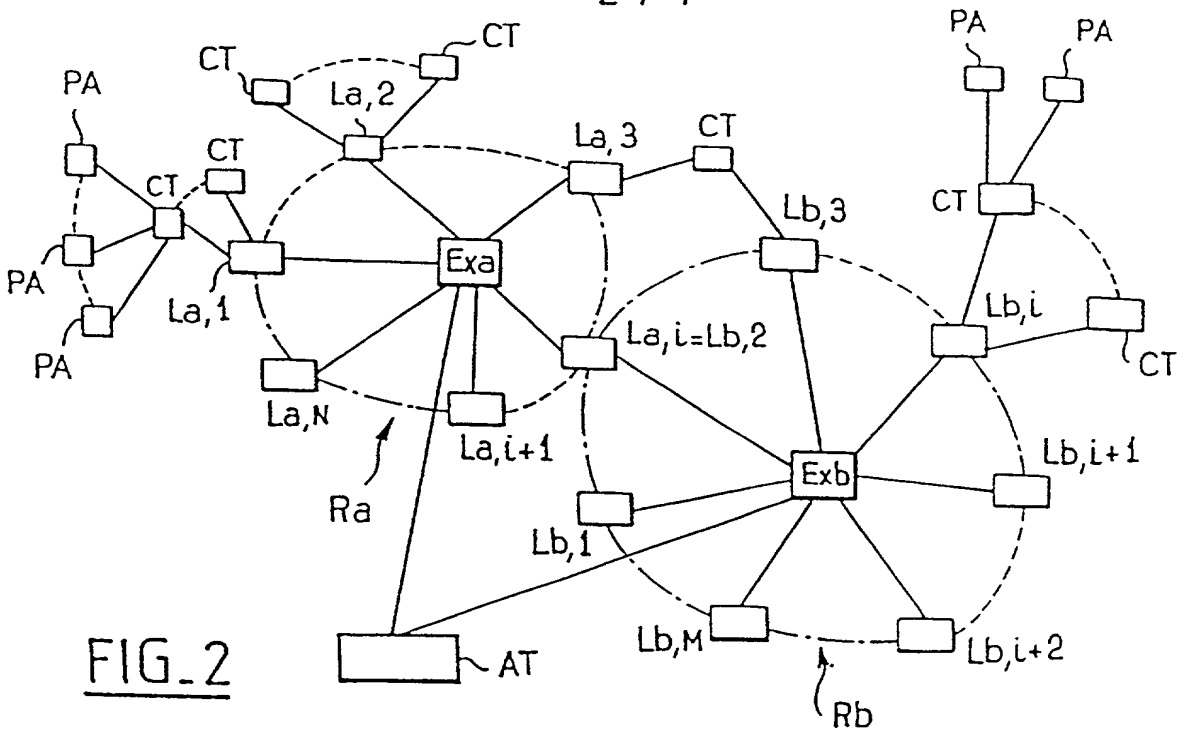
PA
CT
La,2
La,3
Lb,3
Exa
La,1
La,i=Lb,2
Lb,i
La,N
La,i+1
Ra
Exb
Lb,i+1
Lb,1
AT
Lb,M
Lb,i+2
Rb

FIG_2

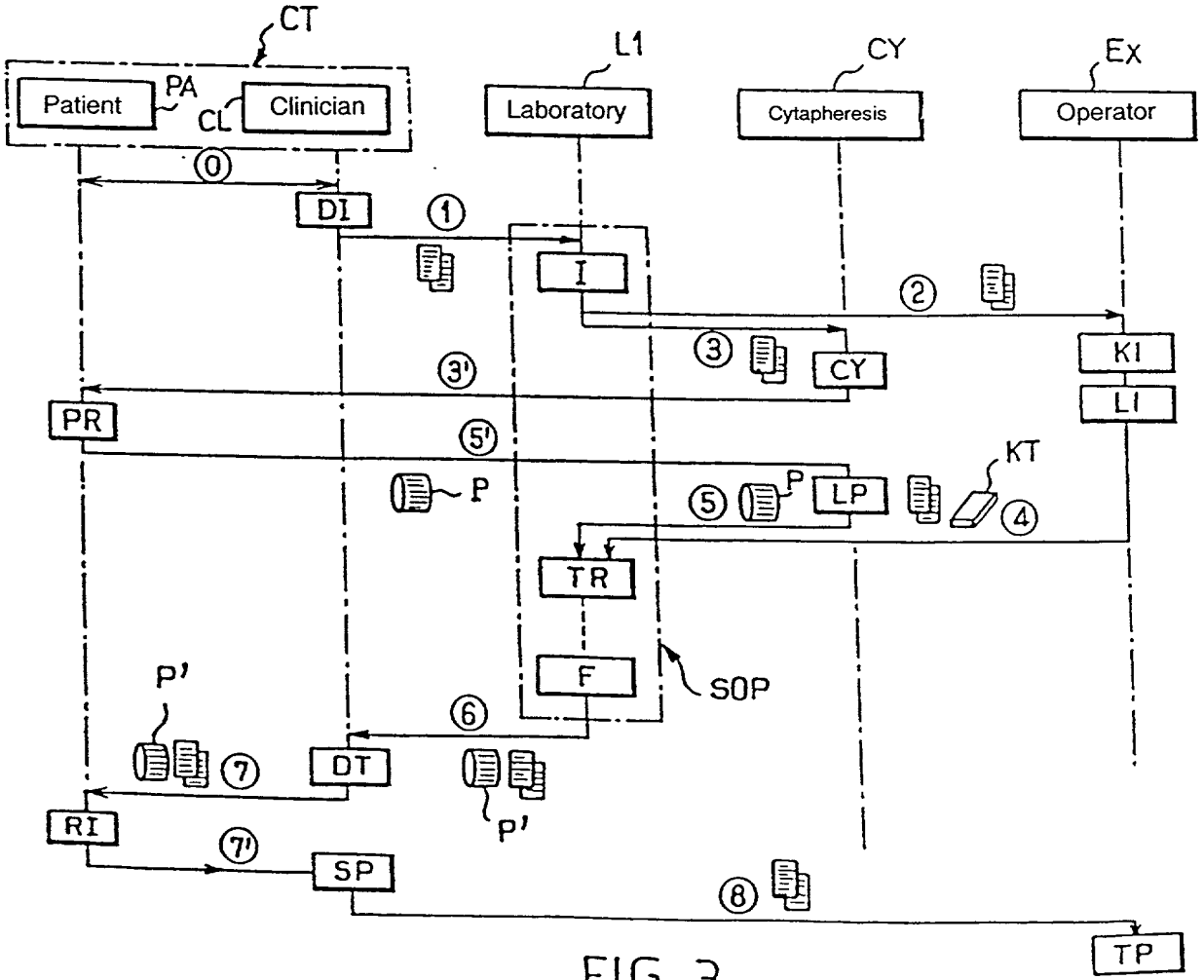
CT
Patient
PA
CL
Clinician
L1
Laboratory
CY
Cytapheresis
Ex
Operator
DI
I
KI
LI
PR
P
KT
LP
TR
F
SOP
P'
DT
RI
SP
TP

FIG_3

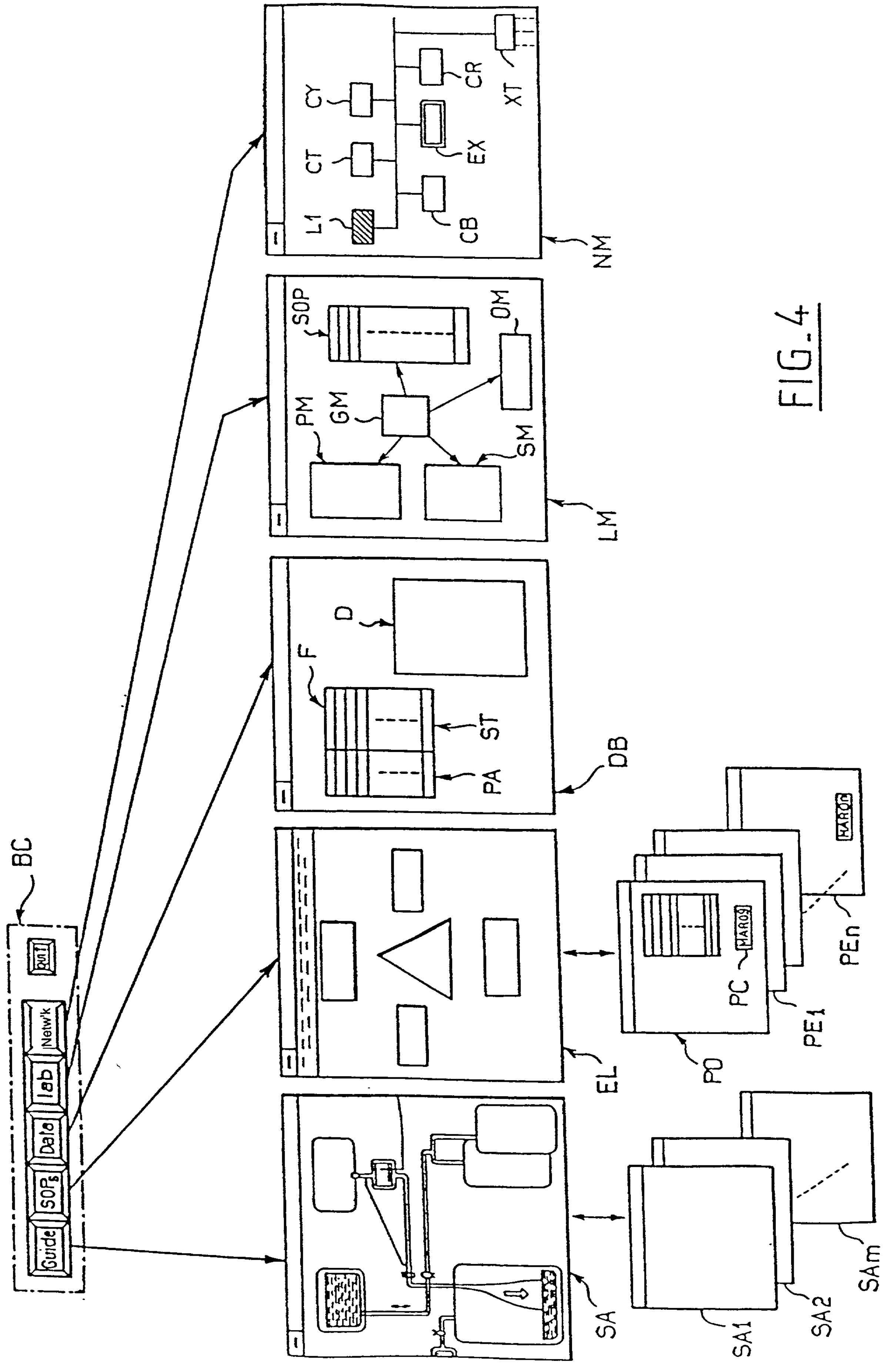
BC
Guide
SOP
Data
lab
Netw'k
SA
SA1
SA2
SAm
EL
PO
PC
MAR09
PE1
PEn
DB
PA
ST
F
D
LM
PM
GM
SM
SOP
OM
NM
L1
CT
CY
CB
EX
CR
XT

FIG. 4

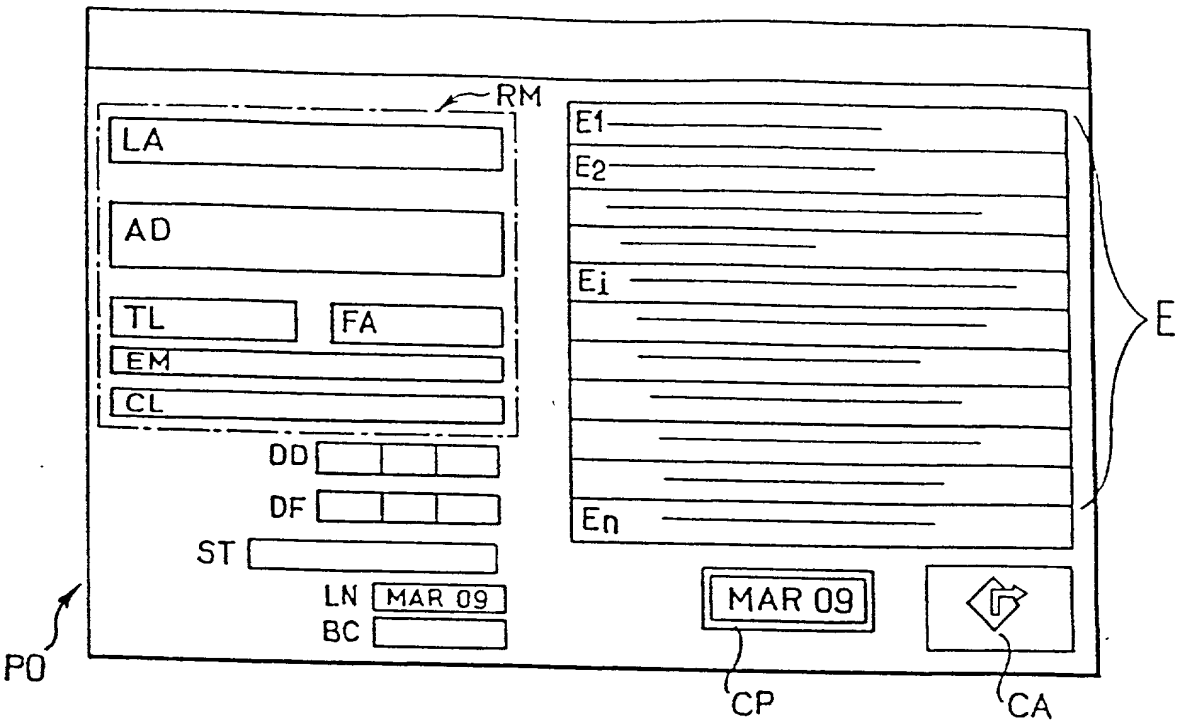
RM
LA
AD
TL
FA
EM
CL
DD
DF
ST
LN
MAR 09
BC
PO
E1
E2
Ei
En
E
MAR 09
CP
CA

FIG_5

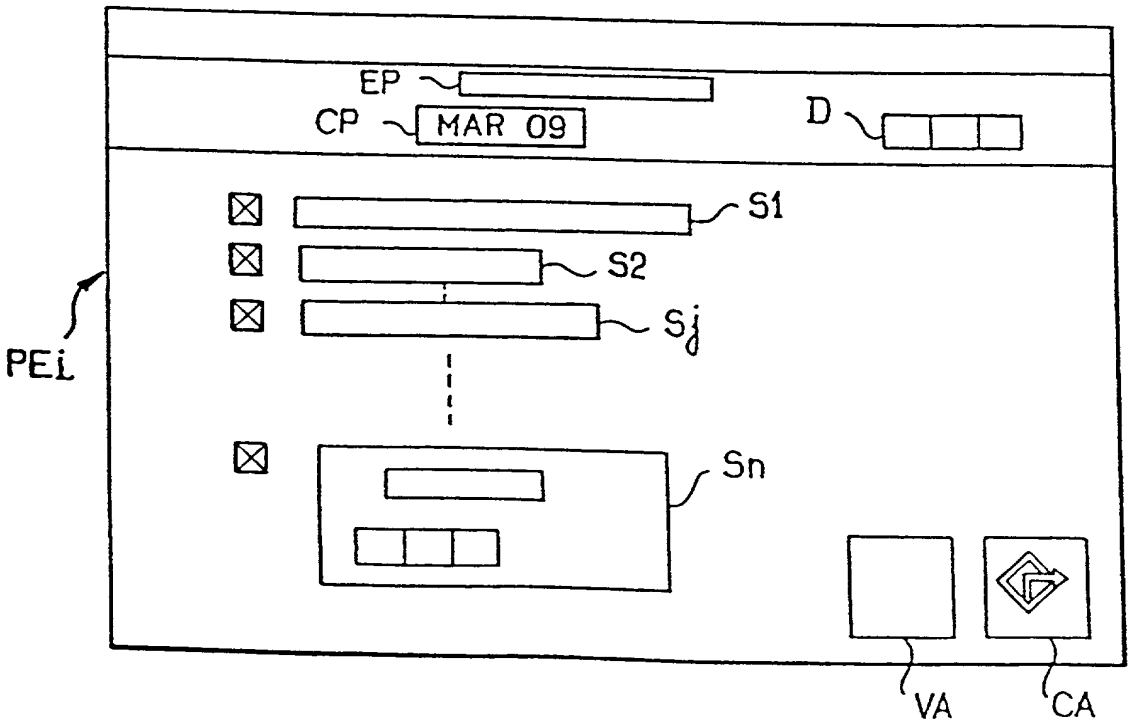
EP
CP
MAR 09
D
S1
S2
Sj
Sn
PEi
VA
CA

FIG_6

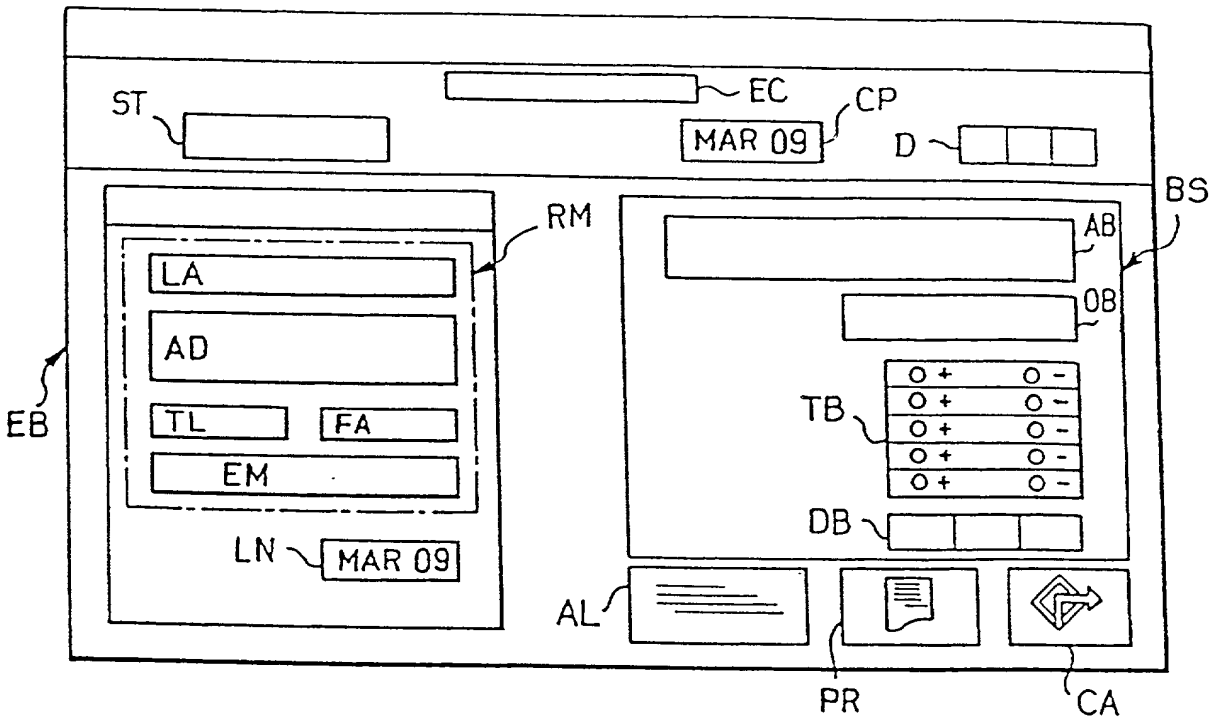
ST
EC
CP
MAR 09
D
BS
RM
AB
LA
OB
AD
TB
EB
TL
FA
EM
DB
LN
MAR 09
AL
PR
CA

FIG_7

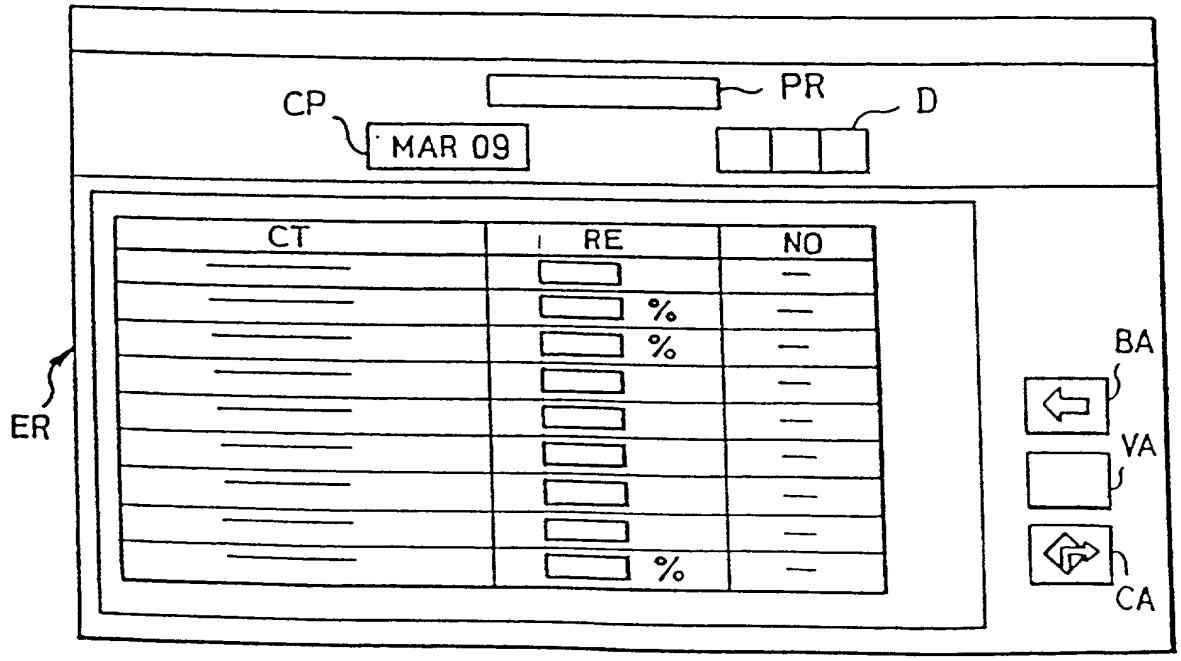
CP
PR
D
MAR 09
CT
RE
NO
ER
BA
VA
CA

FIG_8

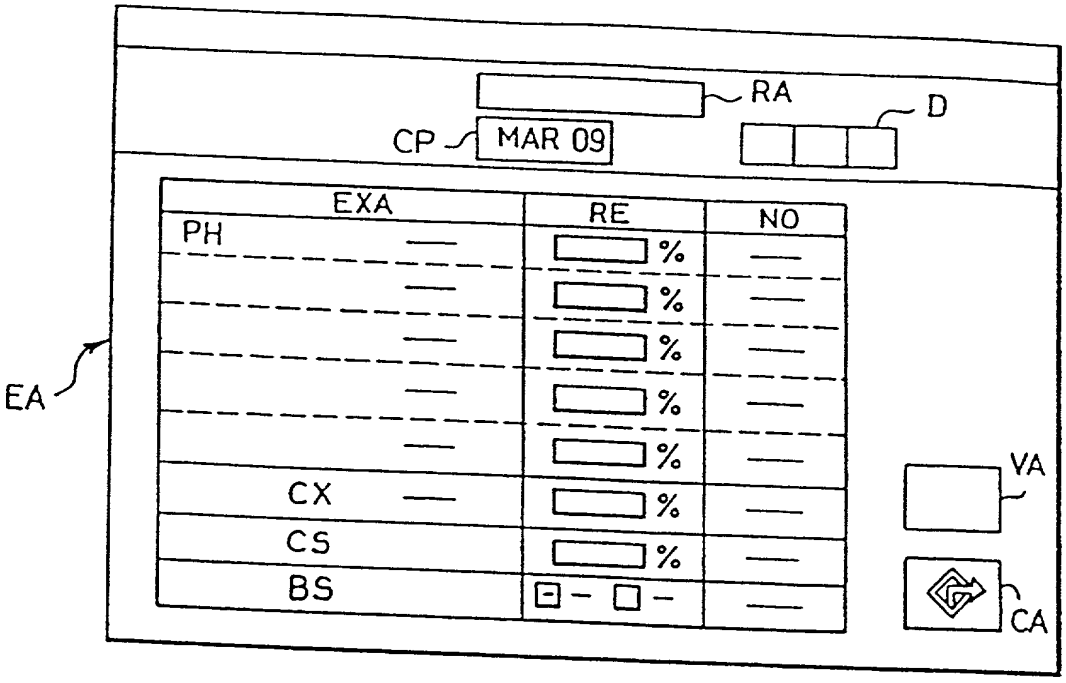
RA
D
CP
MAR 09
EXA
RE
NO
PH
%
CX
CS
BS
EA
VA
CA

FIG_9

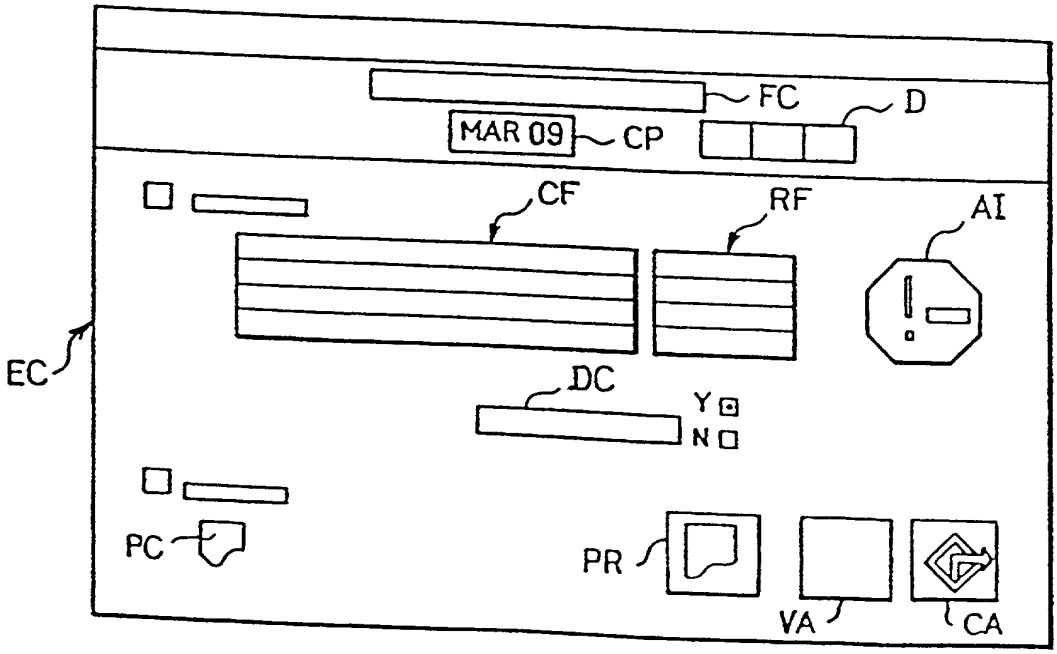
FC
D
MAR 09
CP
CF
RF
AI
EC
DC
Y
N
PC
PR
VA
CA

FIG_10

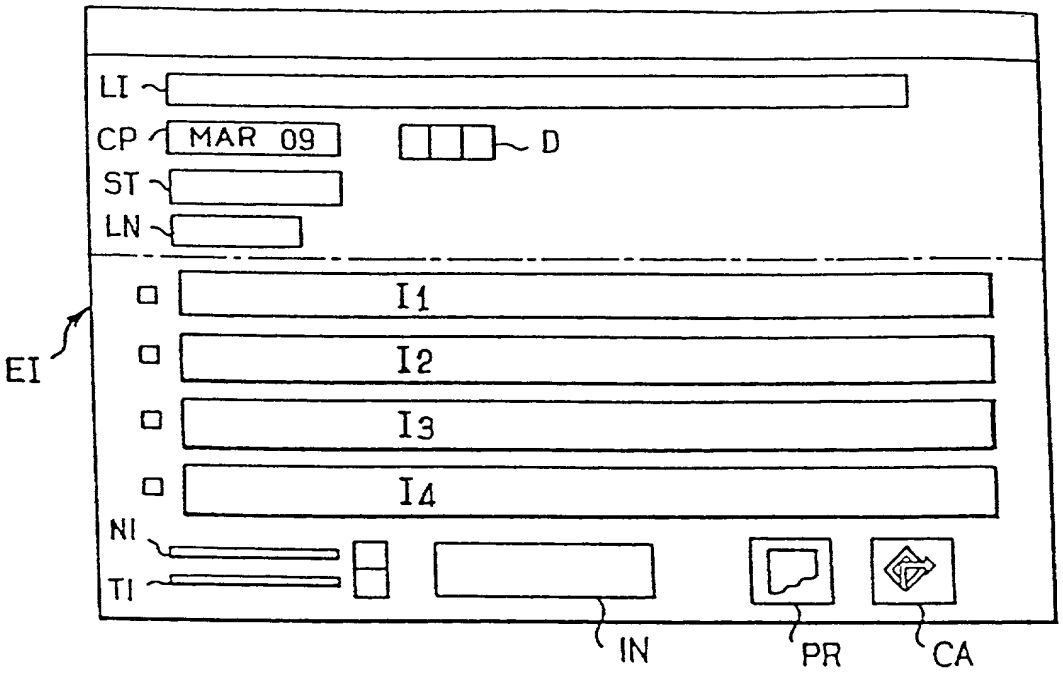
LI
CP
MAR 09
D
ST
LN
EI
I1
I2
I3
I4
NI
TI
IN
PR
CA

FIG_11

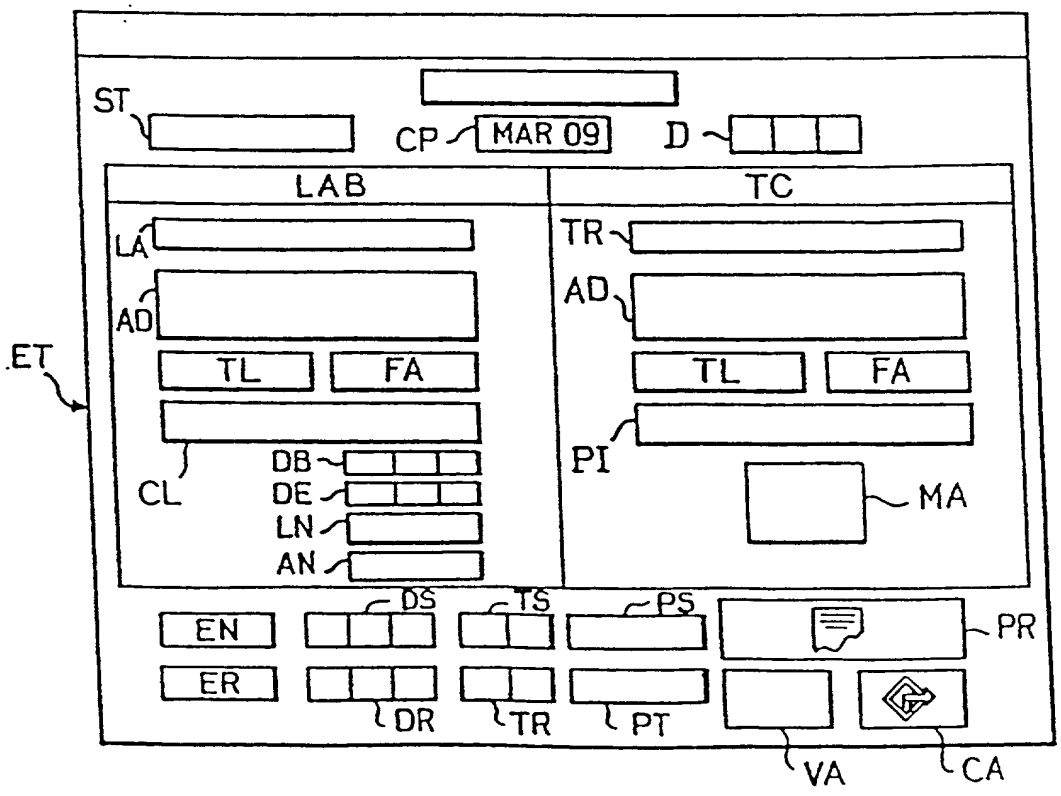
ST
CP
MAR 09
D
LAB
TC
LA
AD
TL
FA
ET
CL
DB
DE
LN
AN
TR
AD
TL
FA
PI
MA
EN
ER
DS
TS
PS
PR
DR
TR
PT
VA
CA

FIG_12

Please type a plus sign (+) inside this box → [+]

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Patent and Trademark Office U.S. DEPARTMENT OF COMMERCE

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DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION

[X] Declaration Submitted with Initial Filing OR [ ] Declaration Submitted after Initial Filing

Attorney Docket Number	410.016
First Named Inventor	Eric THIBAULT et al
COMPLETE IF KNOWN	
Application Number	PCT/FR97/02336
Filing Date	December 17, 1997
Group Art Unit	
Examiner Name	

As a below named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled :

METHOD AND SYSTEM FOR QUALITY MANAGEMENT IN THERAPEUTIC PROCESSES

(Title of the invention)

the specification of which

[ ] is attached hereto

OR

[X] was filed on (MM/DD/YYYY) 12/17/97 as United States Application Number or PCT International Application Number PCT/FR97/02336 and was amended on (MM/DD/YYYY) _____ (if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations, §1.56

I hereby claim foreign priority benefits under Title 35 United States Code §119 (a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365 (a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached? YES	Certified Copy Attached? NO
96/15839	France	12/23/96	[ ]	[ ]	[X]
PCT/FR97/02336	PCT	12/17/97	[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]

[ ] Additional foreign application numbers are listed on a supplemental priority sheet attached hereto

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below

Application Number(s)	Filing Date (MM/DD/YYYY)

[ ] Additional provisional application numbers are listed on a supplemental priority sheet attached hereto.

Please type a plus sign (+) inside this box → [+]

Approved for use through 9/30/98 OMB 0651-0032
Patent and Trademark Office U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

DECLARATION

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s), or §365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number (if applicable)

☐ Additional U.S. or PCT international application numbers are listed on a supplemental priority sheet attached hereto.

As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Name	Registration Number	Name	Registration Number
Bierman, Muserlian and Lucas	18,818		
Jordan B. Bierman	18,629		
Charles A. Muserlian	19,683		
Donald C. Lucas	31,275		

☐ Additional registered practitioner(s) named on a supplemental sheet attached hereto.

Direct all correspondence to:

Name	Charles A. Muserlian				
Address	Bierman, Muserlian and Lucas				
Address	600 Third Avenue				
City	New York	State	NY	ZIP	10016
Country	U.S.A.	Telephone	(212) 661-8000	Fax	(212) 661-8002

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor: ☐ A petition has been filed for this unsigned inventor

Given Name	Middle Initial	Family Name	Suffix e.g. Jr.
Eric		THIBAULT	

Inventor's Signature: [signature] Date: 26/04/1999

Residence: City	State	Country	Citizenship
Jouars-Pontchartrain		France	France

Post Office Address: 5, chemin des Anjoux
F-78760 Jouars-Pontchartrain, France

Post Office Address:

City	State	Zip	Country
Jouars-Pontchartrain		F-78760	France

☒ Additional inventors are being named on supplemental sheet(s) attached hereto

Please type a plus sign (+) inside this box → [+]

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Patent and Trademark Office U S DEPARTMENT OF COMMERCE
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DECLARATION

ADDITIONAL INVENTOR(S) Supplemental Sheet

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name	Jean-Loup	Middle Initial		Family Name	ROMET-LEMONNE	Suffix e.g. Jr.	
Inventor's Signature	[signature]					Date	04/16/1999
Residence: City	Paris FRX	State		Country	France	Citizenship	France
Post Office Address	8, rue de Hesse, F-75003 Paris, France						
Post Office Address							
City	Paris	State		Zip	F-75003	Country	France

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name		Middle Initial		Family Name		Suffix e.g. Jr.	
Inventor's Signature						Date	
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		Zip		Country	

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name		Middle Initial		Family Name		Suffix e.g. Jr.	
Inventor's Signature						Date	
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		Zip		Country	

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name		Middle Initial		Family Name		Suffix e.g. Jr.	
Inventor's Signature						Date	
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		Zip		Country	

☐ Additional inventors are being named on supplemental sheet(s) attached hereto

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☐ Page(s) 4 of 5 - 5 of 5 of Declaration were not present for scanning.
(Document title)

☐ Page(s)_____ of _____ were not present for scanning.
(Document title)

☐ Scanned copy is best available.